



(CASE REPORT)



A late-onset leg rash, unique Janeway lesions or Jarisch-Herxheimer reaction? A case report

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Abstract

Jarisch-Herxheimer reactions typically manifest as a response to antimicrobial therapy for spirochete infections, although these reactions have also been documented following treatment of other microbes. Almost always occurring within 24 hours of treatment initiation, Jarisch-Herxheimer reactions can cause hypotension, fevers, chills, headaches, myalgia, skin rashes, and exacerbations of existing skin lesions, among others; the most feared complication from such reactions is shock. They are usually transient and self-limiting but can cause significant discomfort and concern for patients. Treatment is usually supportive, consisting mostly of nonsteroidal anti-inflammatory drugs (NSAIDs), steroids, and intravenous fluids. Reactions with delayed onset are exceedingly rare, and to our knowledge, have been documented only one other time in literature. In this clinical vignette, we present a case in which a patient developed what we initially suspected to be Janeway lesions; however, the presence of systemic symptoms suggest that what was observed was delayed-onset Jarisch-Herxheimer reaction 16 days after initiation of antibiotics.

Keywords: Jarisch-Herxheimer; Reaction; Syphilis; Rash; Delayed; Onset

1. Introduction

Jarisch-Herxheimer Reaction (JHR) is a phenomenon in which a patient presents with systemic symptoms and lesions after treatment of syphilis. However, rarely does this reaction occur after 24 hours of treatment. Here, we present a case of a 31-year-old woman who initially presented with bacterial endocarditis who developed JHR 16 days after onset of treatment.

2. Case Presentation

A 31-year-old woman with a history of intravenous (IV) heroin use, hepatitis C, and anemia presented to the hospital with two days of diffuse body pain. She described the pain as diffuse but pointed primarily to her lower back. She stated that the pain was unbearable and she could not walk as the weight on her legs exacerbated her lower back pain. Her mother found her on the floor of their home with complaints of not being able to walk or move her legs, which prompted her to call emergency medical services. Her last use of heroin was a day before hospital admission. She denied fever, chills, nausea, vomiting, chest pain, shortness of breath, or diarrhea when she first presented to the hospital.

Computed tomography (CT) thorax showed cavitory lesions suspicious for septic emboli. A trans-thoracic echocardiogram done the day after admission showed a multilobulated vegetation adherent to the anterior tricuspid valve leaflet measuring at least 1.2 x 0.9 centimeters. Trans-esophageal echocardiogram done two days after the previous echocardiogram confirmed findings and showed no mitral valve abnormalities.

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Patient was started on vancomycin and cefepime upon admission. Blood cultures grew methicillin-sensitive *Staphylococcus aureus* on the day of admission, and she was continued on vancomycin and cefepime. She was changed to IV cefazolin on day three. However, she continued to have fevers and elevated white count. She was switched to oxacillin on day five, which improved her fevers. Her blood cultures continued to be positive until day six of hospitalization when cultures came back negative. During this period, her blood pressure remained elevated, which we attributed to continued back pain at that time.

On day seven of hospitalization, the patient developed edema on the right side of her face without airway involvement. Her blood pressure dropped to average 90-100/60-70. Treatment with steroids and antihistamines helped symptoms subside within 48 hours.

On day 16 of hospitalization, she developed non-painful, non-pruritic lesions of the bilateral legs, worse on the right medial leg and calf region, and buttocks. She also complained of swelling of her vagina. Upon inspection, lesions were suspected to be Janeway lesions given her endocarditis. Upon further examination, she had a diffuse rash that gradually became more painful and spared the palms and soles. Further laboratory testing revealed a positive rapid plasma reagin (RPR) with titer elevated greater than 1:16, which strongly suggested syphilis infection. A follow-up Treponemal test was reactive as well. She was ultimately diagnosed with Jarisch-Herxheimer reaction (JHR) in the setting of secondary syphilis.



Figure 1 Multiple lesions seen on the patient's leg on day 16 of hospitalization

3. Discussion

The exact mechanism of JHR is unclear. Herxheimer believed the endotoxin released from the treponemes upon death was the underlying cause¹. Specifically, lipoproteins from spirochetes released from the dying organisms are thought to increase cytokine production, leading to inflammation and the presence of lesions.

JHR reaction is seen in 95% of sero-positive patients in primary syphilis, and this rate of incidence remains as high in early secondary syphilis². The reaction typically onsets very quickly after antimicrobial therapy and resolves without intervention. Patients present with more severe symptoms when the organism is abundant, as in our patient with a titer greater than 1:16³. These symptoms include fever, lesions and edema, and hypertension followed by hypotension. These are all symptoms our patient experienced during hospital stay.

On the other hand, Janeway lesions are associated with bacterial endocarditis and present notably on the hands and soles of feet⁴. Janeway lesions are thought to be caused by microembolization from the thrombus of endocarditis and typically last days to weeks. Although our patient presented with bacterial endocarditis, lesions did not appear until 11 days after blood cultures became consistently negative. Furthermore, her systemic symptoms of fever, edema, and hypertension and later hypotension suggest JHR reaction rather than Janeway lesion as these symptoms persisted despite antibiotic treatment of the endocarditis.

To our knowledge, there is one report of delayed-onset JHR in literature⁵, in which the patient developed symptoms 14 days after treatment with doxycycline. While our patient developed late-onset JHR after treatment with multiple different medications, her systemic symptoms including hypotension and edema occurred after oxacillin treatment. Of note, there is no clear evidence of one particular antibiotic causing JHR¹. Additionally, our patient's presentation is unique in that the lesions present primarily on her legs. We attribute this presentation to the abundance of organisms seen in our patient's titer. Indeed, given that the patient had a titer of greater than 1:16, the likelihood of Jarisch-Herxheimer is as high as 41%⁶. In retrospect, the symptoms this patient presented with after initial treatment of endocarditis could be attributed to JHR.

3.1. Follow-up

The lesions on the patient's legs resolved 72 hours after initial presentation. The patient was treated symptomatically with non-steroid anti-inflammatory drugs. The patient completed a six-week course of antibiotics and was discharged without any further complications.

4. Conclusion

In this clinical vignette, we presented one instance of what we believe may be JHR with delayed onset. Typically occurring within 24 hours of treatment, JHR is usually self-limiting, but it may present disfiguring, uncomfortable, and systemic challenges to afflicted patients. It is our hope that in detailing this particular clinical scenario, we may shed more light on JHR, leading to the precise elucidation of its pathophysiology, as well as novel and effective strategies for treatment and prophylaxis.

Compliance with ethical standards

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The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Disclosure of conflict of interest

The above listed authors have no conflicts of interest to declare.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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